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09/483,831 11/23/96

L22 ANSWER 5 OF 14 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 97382455 MEDLINE
DOCUMENT NUMBER: 97382455
TITLE: Nucleotide binding to autotaxin: crosslinking of bound substrate followed by lysC digestion identifies two labeled peptides.
AUTHOR: Clair T; Krutzsch H C; Liotta L A; Stracke M L
CORPORATE SOURCE: Division of Clinical Sciences, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892, USA.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1997 Jul 18) 236 (2) 449-54.
Journal code: 9Y8. ISSN: 0006-291X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199710

AB **Autotaxin** (ATX) is a 125 kDa glycoprotein **motility** factor and exoenzyme which can catalyze the hydrolysis of either the alpha-beta or at the beta-gamma phosphodiester bond in ATP. Its **motility** stimulating activity requires an intact 5'-nucleotide phosphodiesterase (PDE) active site. Photolysis-dependent labeling of ATX with alpha-[32P]-8-N3-ATP, lysC digestion, and peptide HPLC resolved two radioactive fractions containing single peptides whose amino-terminal **sequences** were determined. Peptide A (T210FPNLYTLATG. . .) was derived from the PDE active site and peptide B (Y318GPFGPEMTNP. . .) was not previously known to be involved in any of the activities of ATX. The differential effect of NaCl concentration on the labeling of these two peptides, as well as on the two reaction types catalyzed by ATX, allows a classification of activities which predicts both the position of preferential peptide labeling by bound ATP and also the position of phosphodiester bond hydrolysis.

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09/483,831 11/23/96 (1020)

L22 ANSWER 4 OF 14 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 97150858 MEDLINE
DOCUMENT NUMBER: 97150858
TITLE: Autotaxin is an exoenzyme possessing 5'-nucleotide phosphodiesterase/ATP pyrophosphatase and ATPase activities.
AUTHOR: Clair T; Lee H Y; Liotta L A; Stracke M L
CORPORATE SOURCE: Laboratory of Pathology, NCI, National Institutes of Health, Bethesda, Maryland 20892, USA.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1997 Jan 10) 272 (2) 996-1001.
Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199704
ENTRY WEEK: 19970403

103

AB **Autotaxin** (ATX) is an extracellular enzyme and an autocrine **motility** factor that stimulates pertussis toxin-sensitive chemotaxis in human melanoma cells at picomolar to nanomolar concentrations. This 125-kDa glycoprotein contains a peptide **sequence** identified as the catalytic site in type I alkaline phosphodiesterases (PDEs), and it possesses 5'-nucleotide PDE (EC 3.1.4.1) activity (Stracke, M. L., Krutzsch, H. C., Unsworth, E. J., Arestad, A., Cioce, V., Schiffmann, E., and Liotta, L. (1992) J. Biol. Chem. 267, 2524-2529; Murata, J., Lee, H. Y., Clair, T., Krutsch, H. C., Arestad, A. A., Sobel, M. E., Liotta, L. A., and Stracke, M. L. (1994) J. Biol. Chem. 269, 30479-30484). ATX binds ATP and is phosphorylated only on threonine. Thr210 at the PDE active site of ATX is required for phosphorylation, 5'-nucleotide PDE, and **motility**-stimulating activities (Lee, H. Y., Clair, T., Mulvaney, P. T., Woodhouse, E. C., Aznavoorian, S., Liotta, L. A., and Stracke, M. L. (1996) J. Biol. Chem. 271, 24408-24412). In this article we report that the phosphorylation of ATX is a transient event, being stable at 0 degrees C but unstable at 37 degrees C, and that ATX has adenosine-5'-triphosphatase (ATPase; EC 3.6.1.3) and ATP pyrophosphatase (EC 3.6.1.8) activities. Thus ATX catalyzes the hydrolysis of the phosphodiester bond on either side of the beta-phosphate of ATP. ATX also catalyzes the hydrolysis of GTP to GDP and GMP, of either AMP or PPi to Pi, and the hydrolysis of NAD to AMP, and each of these substrates can serve as a phosphate donor in the phosphorylation of ATX. ATX possesses no detectable protein kinase activity toward histone, myelin basic protein, or casein. These results lead to the proposal that ATX is capable of at least two alternative reaction mechanisms, threonine (T-type) ATPase and 5'-nucleotide PDE/ATP pyrophosphatase, with a common site (Thr210) for the formation of covalently bound reaction intermediates threonine phosphate and threonine adenylate, respectively.

09/483,831

L22 ANSWER 13 OF 14 MEDLINE DUPLICATE 13
ACCESSION NUMBER: 94218820 MEDLINE
DOCUMENT NUMBER: 94218820
TITLE: The role of autotaxin and other motility stimulating factors in the regulation of tumor cell motility.
AUTHOR: Stracke M; Liotta L A; Schiffmann E
CORPORATE SOURCE: Laboratory of Pathology, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892.
SOURCE: SYMPOSIA OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY, (1993) 47
197-214.
Journal code: VGF. ISSN: 0081-1386.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199407

AB Active cellular **motility** is required for tumor cell penetration of the basement membrane and the interstitial stroma during the transition from in situ to invasive carcinoma. Multiple factors, both autocrine and paracrine in origin, appear to influence this **motile** response. Recently, a potent new cytokine with molecular mass 120 kDa has been purified to homogeneity from a human melanoma cell line (A2058). This new protein, termed **autotaxin** (ATX), is a basic glycoprotein with pI approximately 7.7. ATX is active in the picomolar range, stimulating pertussis toxin sensitive chemotactic and chemokinetic responses by the same cell line that produces it. **Sequence** information, obtained on 11 purified tryptic peptides (114 residues), confirmed that the protein is unique with no significant homology to growth factors or previously described **motility** factors. It is hypothesized that an autocrine **motility** factor, such as ATX, could play a role in the initiation of the metastatic cascade by stimulating tumor cells to move away from the primary tumor. Other **motility** stimulating factors, such as components of the extracellular matrix or growth factors, could then influence both the time course and the localization of tumor cell spread.

L22 ANSWER 12 OF 14 MEDLINE DUPLICATE 12
ACCESSION NUMBER: 95074054 MEDLINE
DOCUMENT NUMBER: 95074054
TITLE: cDNA cloning of the human tumor motility-stimulating protein, autotaxin, reveals a homology with phosphodiesterases.
AUTHOR: Murata J; Lee H Y; Clair T; Krutzsch H C; Arestad A A; Sobel M E; Liotta L A; Stracke M L
CORPORATE SOURCE: Laboratory of Pathology, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1994 Dec 2) 269 (48) 30479-84.
Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
OTHER SOURCE: GENBANK-L35594
ENTRY MONTH: 199503

AB A human cDNA clone encoding **autotaxin**, a tumor cell **motility**-stimulating protein, reveals that this protein is an ecto/exo-enzyme with significant homology to the plasma cell membrane differentiation antigen PC-1. ATX is a 125-kDa glycoprotein, previously isolated from a human melanoma cell line (A2058), which elicits chemotactic and chemokinetic responses at picomolar to nanomolar concentrations. Affinity-purified antipeptide antibodies to the ATX peptide, ATX-102, were employed to screen an A2058 cDNA expression library made in lambda gt11. The partial cDNA sequence which was obtained was then extended by utilizing reverse transcriptase on total cellular RNA followed by polymerase chain reaction amplification. The isolated cDNA clone contained 3251 base pairs, and the mRNA message size was approximately 3.3 kilobases. The deduced **amino acid** sequence of **autotaxin** matched 30 previously sequenced peptides and comprised a protein of 915 **amino acids**. Data base analysis of the ATX sequence revealed a 45% **amino acid** identity (including 30 out of 33 cysteines) with PC-1, a pyrophosphatase/type I phosphodiesterase expressed on the surface of activated B cells and plasma cells. ATX, like PC-1, was found to hydrolyze the type I phosphodiesterase substrate p-nitrophenyl thymidine-5'-monophosphate. **Autotaxin** now defines a novel **motility**-regulating function for this class of ecto/exo-enzymes.

L22 ANSWER 14 OF 14 MEDLINE DUPLICATE 14
ACCESSION NUMBER: 92129337 MEDLINE
DOCUMENT NUMBER: 92129337
TITLE: Identification, purification, and partial sequence analysis of autotaxin, a novel motility-stimulating protein.
AUTHOR: Stracke M L; Krutzsch H C; Unsworth E J; Arestad A; Cioce V; Schiffmann E; Liotta L A
CORPORATE SOURCE: Laboratory of Pathology, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1992 Feb 5) 267 (4) 2524-9.
Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199205

AB **Autotaxin** (ATX) is a potent human **motility**-stimulating protein that has been identified in the conditioned medium from A2058 melanoma cells. This protein has been purified to homogeneity utilizing a strategy involving five column steps. Homogeneity of ATX was verified by two-dimensional gel electrophoresis. The molecular size of ATX is 125 kDa, and it has an isoelectric point of 7.7 +/- 0.2. Purified ATX was digested with cyanogen bromide and trypsin, and the resulting ATX peptides were purified by reverse-phase high performance liquid chromatography. Eleven peptides were subjected to **amino acid** sequence analysis, and 114 residues were identified. The partial **amino acid** sequences and the **amino acid** composition obtained for ATX show that it does not exhibit any significant homology to known growth factors or previously described **motility** factors. At picomolar concentrations, ATX stimulates both random and directed migration of human A2058 melanoma cells. Pretreatment of the melanoma cells with pertussis toxin abolishes the response to purified ATX, indicating that ATX stimulates **motility** through a receptor acting via a pertussis toxin-sensitive G protein.

Microfilm

L22 ANSWER 1 OF 14 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 1999353874 MEDLINE
DOCUMENT NUMBER: 99353874
TITLE: Autotaxin expression in non-small-cell lung cancer.
AUTHOR: Yang Y; Mou Lj; Liu N; Tsao M S
CORPORATE SOURCE: Ontario Cancer Institute and Toronto Hospital-Princess Margaret Hospital, Toronto, Ontario, Canada.
SOURCE: AMERICAN JOURNAL OF RESPIRATORY CELL AND MOLECULAR BIOLOGY,
(1999 Aug) 21 (2) 216-22.
Journal code: AOB. ISSN: 1044-1549.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY WEEK: 19991102

AB **Autotaxin** (ATX) is one of the newly discovered autocrine **motility**-stimulating factors with peptide **sequences** identical to those of the brain-type phosphodiesterase I (PD-Ialpha). Although ATX/PD-Ialpha is believed to play a role in tumor progression, its expression in various human cancers has not been extensively studied. We have studied the expression of ATX messenger RNA (mRNA) in normal human bronchial epithelial cell (HBEC) and non-small-cell lung cancer (NSCLC) cell lines, and in primary NSCLC with their corresponding normal lung tissues, using reverse transcription-polymerase chain reaction, Northern blot analysis, and in situ hybridization. ATX mRNA was commonly expressed in these cell lines and tissues. The predominantly expressed mRNA species corresponded to the ATX complementary DNA isolated from a human teratocarcinoma cell line. Overexpression of ATX mRNA was detected in seven of 12 (58%) tumor cell lines; however, there was no correlation between the levels of expression of ATX mRNA and the spontaneous **motility** of these cells. In situ hybridization localized ATX mRNA expression to the basal cells of normal bronchial epithelium, stromal B lymphocytes, and tumor cells. An overexpression of ATX mRNA as compared with its expression in normal bronchial epithelium was mainly found in poorly differentiated carcinomas. Our findings suggest that ATX may have roles additional to its **motility**-stimulating function in undifferentiated NSCLC.

09/483,831 11/23/96

L22 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 2
ACCESSION NUMBER: 1998:204295 CAPLUS
DOCUMENT NUMBER: 128:267966
TITLE: Autotaxin: a cell motility-stimulating protein useful in cancer diagnosis and therapy
INVENTOR(S): Stracke, Mary; Liotta, Lance; Schiffmann, Elliott; Krutzch, Henry; Murata, Jun
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
SOURCE: U.S., 67 pp. Cont.-in-part of U.S. Ser. No. 249,182, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5731167	A	19980324	US 1994-346455	19941128
US 822043	A0	19930101	US 1992-822043	19920117
US 5449753	A	19950912		
WO 9532221	A2	19951130	WO 1995-US6613	19950524
WO 9532221	A3	19960125		
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TT, UA				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9526038	A1	19951218	AU 1995-26038	19950524
US 6084069	A	20000704	US 1997-977221	19971124
PRIORITY APPLN. INFO.:			US 1992-822043	19920117
			US 1994-249182	19940525
			US 1994-346455	19941128
			WO 1995-US6613	19950524

AB The present invention relates, in general, to autotaxin. In particular, the present invention relates to a DNA segment; cells contg. the recombinant DNA mol.; a method of producing autotaxin; antibodies to autotaxin; and identification of functional domains in autotaxin.

L22 ANSWER 3 OF 14 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 1998214377 MEDLINE
DOCUMENT NUMBER: 98214377
TITLE: Ecto-phosphodiesterase/pyrophosphatase of lymphocytes and non-lymphoid cells: structure and function of the PC-1 family.
AUTHOR: Goding J W; Terkeltaub R; Maurice M; Deterre P; Sali A; Belli S I
CORPORATE SOURCE: Department of Pathology and Immunology, Monash Medical School, Alfred Hospital, Prahran, Victoria, Australia.. goding@med.monash.edu.au
SOURCE: IMMUNOLOGICAL REVIEWS, (1998 Feb) 161 11-26. Ref: 98
Journal code: GG4. ISSN: 0105-2896.
PUB. COUNTRY: Denmark
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199807
ENTRY WEEK: 19980705

AB Many developmentally regulated membrane proteins of lymphocytes are ecto-enzymes, with their active sites on the external surface of the cell.

These enzymes commonly have peptidase, phosphodiesterase or nucleotidase activity. Their biological roles are just beginning to be discovered. Although their expression is usually associated with particular stages of lymphoid differentiation, the same gene products are often expressed on the surface of certain non-lymphoid cell types outside the immune system, indicating that their functions cannot be unique to lymphocytes, nor can they be ubiquitous. The plasma cell membrane protein PC-1 (phosphodiesterase I; EC 3.1.4.1/nucleotide pyrophosphatase; EC 3.6.1.9), which was one of the first serological markers for lymphocyte subsets to be discovered, is a typical example. Within the immune system, PC-1 is confined to plasma cells, which represent about 0.1% of lymphocytes. However, PC-1 is also expressed on cells of the distal convoluted tubule of the kidney, chondrocytes, osteoblasts, epididymis and hepatocytes. Recent work has shown that PC-1 is a member of a multigene family of ecto-phosphodiesterases that currently has two other members, PD-1 alpha (**autotaxin**) and PD-1 beta (B10). Within this family, the extracellular domains are highly conserved, especially around the active site. In contrast, the transmembrane and cytoplasmic domains are highly divergent. Individual members of the eco-phosphodiesterase family have distinct patterns of distribution in different cell types, and even within the same cell. For example, PC-1 is present only on the basolateral surface of hepatocytes, while B10 (PD-1 beta) is confined to the apical surface. Analysis of conservation and differences in the **sequence** of their cytoplasmic tails may illuminate intracellular targetting signals. Ecto-phosphodiesterases may play a part in diverse activities in different tissues, including recycling of nucleotides. They may also regulate the concentration of pharmacologically active extracellular compounds such as adenosine or its derivatives and cell **motility**. Some members may modulate local concentrations of pyrophosphate, and

hence influence calcification in bone and cartilage.

L22 ANSWER 6 OF 14 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 96411712 MEDLINE
DOCUMENT NUMBER: 96411712
TITLE: Site-directed mutagenesis of nm23-H1. Mutation of proline 96 or serine 120 abrogates its motility inhibitory activity upon transfection into human breast carcinoma cells.
AUTHOR: MacDonald N J; Freije J M P; Stracke M L; Manrow R E; Steeg P S
CORPORATE SOURCE: Women's Cancers Section, Laboratory of Pathology, Division of Clinical Sciences, NCI, National Institutes of Health, Bethesda, Maryland 20892, USA.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 Oct 11) 271 (41) 25107-16.
Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
OTHER SOURCE: GENBANK-X17620
ENTRY MONTH: 199701
ENTRY WEEK: 19970104

AB We report the first correlation of Nm23 sequence and its tumor metastasis-suppressive capacity using site-directed mutagenesis and an in vitro tumor cell **motility** assay. MDA-MB-435 human breast carcinoma cells were transfected with a control expression vector (pCMVBamneo), the vector containing the wild type nm23-H1, or the nm23-H1 vector encoding mutations at the following **amino acids** : serine 44, a phosphorylation site; proline 96, the k-pn mutation in the Drosophila nm23 homolog that causes developmental defects; histidine 118, involved in Nm23's nucleoside diphosphate kinase activity; and serine 120, a site of mutation in human neuroblastomas and phosphorylation. The wild type nm23-H1 transfectants were 44-98% less **motile** to serum and 86-99% less **motile** to **autotaxin** than control vector transfectants. The proline 96 k-pn, serine 120 to glycine, and to a lesser extent serine 120 to alanine mutant nm23-H1-transfected cell lines exhibited **motility** levels at or above the control transfectants, indicating that these mutations can abrogate the **motility** -suppressive phenotype of nm23-H1. No effect was observed on cellular proliferation, nor were the serine 44 to alanine nm23-H1 mutant transfectants **motile**, demonstrating the specificity of the data. The data identify the first structural motifs of nm23-H1 that influence its metastasis suppressive effect and suggest complex biochemical associations or activities in the Nm23 suppressive pathway.

L22 ANSWER 7 OF 14 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 96394591 MEDLINE
DOCUMENT NUMBER: 96394591
TITLE: Stimulation of tumor cell motility linked to phosphodiesterase catalytic site of autotaxin.
AUTHOR: Lee H Y; Clair T; Mulvaney P T; Woodhouse E C; Aznavoorian S; Liotta L A; Stracke M L
CORPORATE SOURCE: Laboratory of Pathology, NCI, National Institutes of Health, Bethesda, Maryland 20892, USA.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 Oct 4) 271 (40) 24408-12.
Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199701
ENTRY WEEK: 19970104

AB A family of extracellular type I phosphodiesterases has recently been isolated by cDNA cloning, but a physiological function linked to the phosphodiesterase active site has remained unknown. We now present evidence that the phosphodiesterase catalytic site, 201YMRPVYPTKTFPN213, is essential for the **motility** stimulating activity of **autotaxin** (ATX), one member of the exophosphodiesterase family. Native ATX possesses phosphodiesterase activity at neutral and alkaline pH, binds ATP noncovalently, and undergoes threonine phosphorylation. Homogeneously purified recombinant ATX, based on the teratocarcinoma sequence, retains these same activities. A single **amino acid** in the phosphodiesterase catalytic site, Thr210, is found to be necessary for **motility** stimulation, phosphodiesterase activity, and phosphorylation. Two mutant recombinant proteins, Ala210- and Asp210-ATX, lack **motility** stimulation and lack both enzymatic activities; Ser210-ATX possesses intermediate activities. Another mutation, with the adjacent lysine (Lys209) changed to Leu209-ATX, possesses normal **motility** stimulation with sustained phosphodiesterase activity but exhibits no detectable phosphorylation. This mutation eliminates the phosphorylation reaction and indicates that the dephosphorylated state is an active **motility**-stimulating form of the ATX molecule. By demonstrating that the phosphodiesterase enzymatic site is linked to **motility** stimulation, these data reveal a novel role for this family of exo/ecto-enzymes and open up the possibility of extracellular enzymatic cascades as a regulatory mechanism for cellular **motility**.

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L22 ANSWER 8 OF 14 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 96158950 MEDLINE
DOCUMENT NUMBER: 96158950
TITLE: Cloning, chromosomal localization, and tissue expression of autotaxin from human teratocarcinoma cells.
AUTHOR: Lee H Y; Murata J; Clair T; Polymeropoulos M H; Torres R; Manrow R E; Liotta L A; Stracke M L
CORPORATE SOURCE: Laboratory of Pathology, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892, USA.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1996 Jan 26) 218 (3) 714-9.
Journal code: 9Y8. ISSN: 0006-291X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
OTHER SOURCE: GENBANK-L46720
ENTRY MONTH: 199605

AB **Autotaxin**, a potent human tumor cell **motility** -stimulating exophosphodiesterase, was isolated and cloned from the human teratocarcinoma cell line NTera2D1. The deduced **amino acid** sequence for the teratocarcinoma **autotaxin** has 94% identity to the melanoma-derived protein, 90% identity to rat brain phosphodiesterase I/nucleotide pyrophosphatase (PD-I alpha), and 44% identity to the plasma cell membrane marker PC-I. Utilizing polymerase chain reaction screening of the CEPH YAC library, we localized the **autotaxin** gene to human chromosome 8q23-24. Northern blot analysis of relative mRNA from multiple human tissues revealed that **autotaxin** mRNA steady state expression is most abundant in brain, placenta, ovary, and small intestine.

L22 ANSWER 9 OF 14 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 97127417 MEDLINE
DOCUMENT NUMBER: 97127417
TITLE: Treatment of fibroblast-like synoviocytes with IFN-gamma results in the down-regulation of autotaxin mRNA.
AUTHOR: Santos A N; Riemann D; Santos A N; Kehlen A; Thiele K; Langner J
CORPORATE SOURCE: Institute of Med. Immunology, Martin Luther University Halle-Wittenberg, Germany.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1996 Dec 13) 229 (2) 419-24.
Journal code: 9Y8. ISSN: 0006-291X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
OTHER SOURCE: GENBANK
ENTRY MONTH: 199703
ENTRY WEEK: 19970304

AB In an effort to isolate genes that change expression at the mRNA level during treatment of fibroblast-like synoviocytes (SFC) with IFN-gama, we performed a differential display analysis. Here, we report the isolation of a cDNA clone corresponding to a 3.1 kb mRNA species that is reduced in synoviocytes after culture with IFN-gama. **Sequence** analysis revealed the 211 bp length cDNA clone to be identical to the **motility**-stimulating 125 kDa protein **autotaxin** (ATX). The down-regulation of ATX mRNA was confirmed by Northern blot analysis as well as competitive RT-PCR. SFC express 1 ng ATX mRNA/microgram total RNA. IFN-gama down-regulated ATX mRNA up to 50% as compared to control. Our results add a new finding to the manifold functions described for IFN-gama in rheumatoid arthritis.

L22 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 10
ACCESSION NUMBER: 1996:520573 CAPLUS
DOCUMENT NUMBER: 125:239670
TITLE: Molecular cloning of rat intestinal phosphodiesterase I/nucleotide pyrophosphatase (PD-I.beta.)
AUTHOR(S): Terashima, Kazuhiro
CORPORATE SOURCE: Sch. Med., Kobe Univ., Kobe, 650, Japan
SOURCE: Kobe Daigaku Igakubu Kiyo (1996), 56(2-4), 109-114
CODEN: KDIKAX; ISSN: 0075-6431
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB Phosphodiesterase I/nucleotide pyrophosphatase is a widely expressed ectoenzyme. Its extracellular domain cleaves pyrophosphate, phosphodiester, and phosphosulfate linkages. From chromatog. study there are at least 5 isoenzymes in this enzyme. The plasma cell antigen, PC-1, belongs to this family and accumulating evidence has suggested its role in pathophysiol. of various human diseases including diabetes mellitus and bone diseases. We have previously cloned brain-type enzyme and designated PD-I.alpha.. Later found that PDI.alpha. is identical with tumor cell **motility**-stimulating factor, **Autotaxin**. In this study we have cloned cDNA encoding intestinal enzyme from rat small intestine cDNA library and designated PD-I.beta.. The isolated cDNA clone contained 2744 base pairs. The deduced **amino acid** comprised a protein of 876 **amino acids** and calcd. mol. wt. was 99.322 Da. There were single transmembrane domain, putative enzymic catalytic site, somatomedin B-like domain, arginine-glycine-aspartate (RGD) motif, and calcium binding EF hand motif. The identification of PD-I.beta. may provide a novel mol. tool to further understand the role of ecto-phosphodiesterase I/nucleotide pyrophosphatase.

L22 ANSWER 11 OF 14 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 96163899 MEDLINE
DOCUMENT NUMBER: 96163899
TITLE: Molecular cloning and chromosomal assignment of the human brain-type phosphodiesterase I/nucleotide pyrophosphatase gene (PDNP2).
AUTHOR: Kawagoe H; Soma O; Goji J; Nishimura N; Narita M; Inazawa J; Nakamura H; Sano K
CORPORATE SOURCE: Department of Pediatrics, Kobe University School of Medicine, Japan.
SOURCE: GENOMICS, (1995 Nov 20) 30 (2) 380-4.
Journal code: GEN. ISSN: 0888-7543.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-D45421; GENBANK-D45914
ENTRY MONTH: 199605

AB Phosphodiesterase I/nucleotide pyrophosphatase is a widely expressed membrane-bound enzyme that cleaves diester bonds of a variety of substrates. We have cloned brain-type cDNA for this enzyme from rat brain and designated it PD-I alpha (M. Narita, J. Goji, H. Nakamura, and K. Sano, 1994, J. Biol. Chem. 269: 28235-28242). In this study we have isolated cDNA and genomic DNA encoding human PD-I alpha. Human PD-I alpha cDNA, designated PDNP2 in HGMW nomenclature, has a 2589-nucleotide open reading frame encoding a polypeptide of 863 **amino acids** with a calculated M(r) of 99,034. Northern blot analysis revealed that human PD-I alpha transcript was present in brain, lung, placenta, and kidney. The database analysis showed that human PD-I alpha was identical with human **autotaxin** (ATX), a novel tumor **motility** -stimulating factor, except that human PD-I alpha lacks 156 nucleotides and 52 **amino acids** of human ATX. Human PD-I alpha and human ATX are likely to be alternative splicing products from the same gene. The 5' region of the human PDNP2 gene contains four putative binding sites of transcription factor Sp1 without typical TATA or CAAT boxes, and there is a potential octamer binding motif in intron 2. From the results of fluorescence in situ hybridization, the human PDNP2 gene is located at chromosome 8q24.1.

L23 ANSWER 1 OF 2 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 95074054 MEDLINE
DOCUMENT NUMBER: 95074054
TITLE: cDNA cloning of the human tumor motility-stimulating protein, autotaxin, reveals a homology with phosphodiesterases.
AUTHOR: Murata J; Lee H Y; Clair T; Krutzsch H C; Arestad A A; Sobel M E; Liotta L A; Stracke M L
CORPORATE SOURCE: Laboratory of Pathology, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1994 Dec 2) 269 (48) 30479-84.
Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
OTHER SOURCE: GENBANK-L35594
ENTRY MONTH: 199503

AB A human cDNA clone encoding **autotaxin**, a tumor cell **motility**-stimulating protein, reveals that this protein is an ecto/exo-enzyme with significant homology to the plasma cell membrane differentiation antigen PC-1. ATX is a 125-kDa glycoprotein, previously isolated from a human melanoma cell line (A2058), which elicits chemotactic and chemokinetic responses at picomolar to nanomolar concentrations. Affinity-purified antipeptide antibodies to the ATX peptide, ATX-102, were employed to screen an A2058 cDNA expression library made in lambda gt11. The partial cDNA sequence which was obtained was then extended by utilizing reverse transcriptase on total cellular RNA followed by polymerase chain reaction amplification. The isolated cDNA clone contained 3251 base pairs, and the mRNA message size was approximately 3.3 kilobases. The deduced **amino acid** sequence of **autotaxin** matched 30 previously sequenced peptides and comprised a protein of 915 **amino acids**. Data base analysis of the ATX sequence revealed a 45% **amino acid** identity (including 30 out of 33 cysteines) with PC-1, a pyrophosphatase/type I phosphodiesterase expressed on the surface of activated B cells and plasma cells. ATX, like PC-1, was found to hydrolyze the type I phosphodiesterase substrate p-nitrophenyl thymidine-5'-monophosphate. **Autotaxin** now defines a novel **motility**-regulating function for this class of ecto/exo-enzymes.

DUP

L23 ANSWER 2 OF 2 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 92129337 MEDLINE
DOCUMENT NUMBER: 92129337
TITLE: Identification, **purification**, and partial sequence analysis of autotaxin, a novel motility-stimulating protein.
AUTHOR: Stracke M L; Krutzsch H C; Unsworth E J; Arestad A; Cioce V; Schiffmann E; Liotta L A
CORPORATE SOURCE: Laboratory of Pathology, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1992 Feb 5) 267 (4) 2524-9.
Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199205

AB **Autotaxin** (ATX) is a potent human **motility**-stimulating protein that has been identified in the conditioned medium from A2058 melanoma cells. This protein has been purified to homogeneity utilizing a strategy involving five column steps. Homogeneity of ATX was verified by two-dimensional gel electrophoresis. The molecular size of ATX is 125 kDa, and it has an isoelectric point of 7.7 +/- 0.2. Purified ATX was digested with cyanogen bromide and trypsin, and the resulting ATX peptides were purified by reverse-phase high performance liquid chromatography. Eleven peptides were subjected to **amino acid** sequence analysis, and 114 residues were identified. The partial **amino acid** sequences and the **amino acid** composition obtained for ATX show that it does not exhibit any significant homology to known growth factors or previously described **motility** factors. At picomolar concentrations, ATX stimulates both random and directed migration of human A2058 melanoma cells. Pretreatment of the melanoma cells with pertussis toxin abolishes the response to purified ATX, indicating that ATX stimulates **motility** through a receptor acting via a pertussis toxin-sensitive G protein.

L28 ANSWER 1 OF 3 MEDLINE
ACCESSION NUMBER: 1998277951 MEDLINE
DOCUMENT NUMBER: 98277951
TITLE: Production of a motility factor by a newly established lung adenocarcinoma cell line.
AUTHOR: Klominek J; Robert K H; Bergh J; Hjerpe A; Gahrton G; Sundqvist K G
CORPORATE SOURCE: Department of Lung Medicine, Huddinge University Hospital, Sweden.. Julius.Klominek@impi.ki.se
SOURCE: ANTICANCER RESEARCH, (1998 Mar-Apr) 18 (2A) 759-67. Journal code: 59L. ISSN: 0250-7005.
PUB. COUNTRY: Greece
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199808
ENTRY WEEK: 19980803

AB We have established and characterised a cell line, designated WART, from a patient with primary adenocarcinoma of the lung. This cell line grows with a doubling time of approximately 15 hours, forms colonies in soft agarose, is tumorigenic in athymic nude mice, and has a complex karyotype with both structural and numerical abnormalities. WART serum free conditioned medium (SFCM) contains a factor which stimulates motile behavior of WART cells. This factor with an apparent molecular weight of 67 kDa induced in an autocrine fashion prominent pseudopodia, and chemotactic and chemokinetic responses. Heparin affinity chromatography, ion exchange and molecular sieve chromatography accompanied by SDS-PAGE analysis showed that the motility inducing activity was associated with a major band with molecular weight 67 kDa. The motility inducing activity of the 67 kDa protein was not sensitive to reduction with either dithiotreitol or mercaptoethanol which distinguishes it from A-2058 melanoma autocrine motility factor (AMF)/**autotaxin**, HT-1080 fibrosarcoma AMF and scatter factor which lose their biological activity upon reduction. This 67 kDa motility inducing factor did not augment DNA synthesis indicating that its locomotor activity is independent of mechanisms regulating cell growth. Pertusis toxin inhibited the motile response induced by the 67 kDa protein indicating a signal transduction pathway involving G proteins. Due to its production of the motility stimulating protein the cell line could facilitate studies of invasion and metastasis of human lung tumors.